

**Description of Replacement Drawings:**

The attached sheets of drawings include Figs. 1-15, which replace the originally filed sheets.

Applicants respectfully assert that none of the drawings have been amended with respect to content, and any format changes have been made to comply with 37 CFR §1.121(d).

Attachment: 17 Replacement Sheets

**REMARKS**

Applicants wish to thank the Examiner for the personal interview conducted on 6/22/2005, where agreement was not reached with respect to patentable claims over the prior art of record but the Examiner indicated that the proposed claim amendments may overcome the 35 U.S.C. §102 prior art rejections although the rejections under 35 U.S.C. §103(a) may still apply. The interview was conducted in person and attended by Examiners Marjorie A. Moran and Marina I. Miller, and Applicants' representative William R. McCarthy III. The subject matter of the interview included a general discussion of the Examiners point of view regarding utility under 35 U.S.C. §101 and bioinformatic inventions, Applicants indication of support for claims in priority documents, as well as discussion of proposed claim amendments which were faxed to the Examiner prior to the interview. In particular, the limitations of iteratively fitting a one or more intensity values to a model of independent claims 1 and 3 were discussed with respect to the rejections applied under 35 U.S.C. §102(b) and 35 U.S.C. §103(a) and in particular the disclosure of Hu et al. (*Genome Research*, 11(7):1237-45 (July 2001)). Applicants would like to state that the interview was found to be very helpful in advancing the prosecution of the present application.

Upon entry of this amendment claims 1-5, 7, 11-21, 24-25, 28-37, 40-41 and 43-45 are pending, and of these claims 1, 3, 28, and 43 are independent. Applicants have cancelled claims 6, 8-10, 22-23, 26-27, 38-39, and 42.

Applicants have amended paragraphs 0074 and 0076 to remove the embedded hyperlinks. Applicants also gladly provide another copy of the originally filed Oath/Declaration for the Examiner which is attached herewith.

Applicants have amended claims 1, 3, 28, and 43 to include the limitations of the probe-set identifiers that each identify a probe-set disposed on one or more probe arrays, the support for which may be found in paragraph 0081 *et seq.* of the present application and the limitation of the intensity values detected from each of probe-set, the support for which may be found in paragraph 0063 *et seq.* of the present application. Also, Applicants have amended each of the aforementioned claims to include the limitations of determining one or more alternative splice variants by iteratively fitting the probe-set identifiers and intensity values to a plurality of models of known genomic structure each associated with the alternative splice variants, where the fit of one or more of the models to the probe-set identifiers and intensity data indicates the presence of the alternative splice variants, the support for which may be found in paragraph 00119 *et seq.* of the present application.

Applicants have also amended claims 1 and 31 (Applicants have cancelled claim 8) in accordance with the election of “nucleic acids” with respect to species A; claims 16-17, 33-34, and 44-45 in accordance with the election of “mRNA” with respect to species C; claims 18, 20, and 21 in accordance with the election of graphically associating with respect to the enabling mode of species D. Applicants have cancelled claim 9 which corresponded to species B.

Applicants assert that no new matter is presented by these amendments and respectfully request entry of the same.

Reply to Claim Rejections – 35 U.S.C. §101

Claims 1, 3-9, and 11-45 are rejected under 35 U.S.C. §101.

Applicants respectfully assert that claims 1, 3, 28, and 43 as amended each comply with the requirements of 35 U.S.C. §101 as discussed in the personal interview of 6/22/2005. In particular, each of the aforementioned claims as amended provides a concrete, tangible and useful result that has practical application. For example, the claims are concrete because they include a user defined selection that clearly sets forth the set of data acted upon from the world of possibilities, and also produces a clear result that is specific, substantial, and credible, such as one or more alternative splice variants and correlated annotation datum. Further, the result produced is tangible by providing the alternative splice variants, and correlated annotation datum to a user over an internet network. Additionally, those of ordinary skill in the related art will appreciate what alternative splice variants are, as well as the usefulness of identifying alternative splice variants by employing the advantages provided by probe arrays and correlating the alternative splice variants with annotation data.

Therefore, Applicants respectfully assert that each of claims 1, 3, 28, and 43 are directed to statutory subject matter and comply with 35 U.S.C. §101 and are thus patentable. Additionally, Applicants assert that each of claims 4-5, 7, 11-21, 24-25, 29-37, 40-41, and 44-45 each depend from either claims 1, 3, 28, or 43 and are thus also patentable for the same reasons.

#### Reply to Claim Rejections – 35 U.S.C. §102

Claims 1, 3, 4, 6-9, 11, 12, 16-22, 24-28, 31, 33-37, and 40-42 are rejected under 35 U.S.C. §102(b) over Hu et al. (*Genome Research*, 11(7):1237-45 (July 2001)). Hu et al. is generally directed to the detection of tissue-specific splice variants using high-

density oligonucleotide arrays, where the splice variants are detected using two algorithms for normalizing and comparing hybridization signals at the probe level.

Applicants respectfully assert that the disclosure of Hu et al. does not describe all of the limitations of independent claims 1, 3, 28, and 43 as amended. In particular, Applicants assert that Hu et al. does not describe the limitations of iteratively fitting a user selection of one or more probe-set identifiers, and one or more intensity values to a plurality of models of known genomic structure each associated with one of the alternative splice variants. Rather, Hu et al. describes the prediction of tissue-specific splice variants by first calculating a relative signal strength (RSS) value for pairs of probes (i.e. one probe perfectly matched to the target sequence, and one with a mismatch between the probe and target sequences) and comparing the RSS values associated with the same target sequence between different tissue types. There is no description in Hu et al. of iterative fitting of any data, nor is there description of models of known genomic structure that are associated with alternative splice variants. Therefore, Hu et al. also does not describe that the fit of the probe-set identifiers and intensity values to one or more of the models indicates the presence of the alternative splice variants.

Applicants respectfully assert that Hu et al. does not teach the combination of elements of independent claims 1, 3, 28, and 43 and are thus each patentable for the reasons given above and request that the rejection be withdrawn. Additionally, Applicants assert that each of claims 4, 6-9, 11-12, 16-22, 24-27, 31-33-37, and 40-42 depend from either claims 1, 3, or 28 and are thus also patentable for the same reasons.

Claims 43-45 are rejected under 35 U.S.C. §102(a) and (e) over Wang et al.(U.S. Patent Application Publication Serial No. 2002/0029113). Applicants respectfully point out that the description of Wang et al. is complementary to the description provided by Hu et al. as described above.

As described above with respect to the rejection under 35 U.S.C. §102(b) and the disclosure of Hu et al., Applicants respectfully assert that the disclosure of Wang et al. does not describe all of the limitations of independent claim 43 as amended. Applicants respectfully assert that Wang et al. does not describe the limitations of iteratively fitting a user selection of one or more probe-set identifiers and one or more intensity values to a plurality of models of known genomic structure associated with the alternative splice variants. Similar to the description of Hu et al., Wang et al. does not describe iterative fitting of any data, or models of known genomic structure that are associated with alternative splice variants.

Applicants respectfully assert that Wang et al. does not teach the combination of elements of independent claim 43 and is thus patentable for the reasons given above and request that the rejection be withdrawn. Applicants also assert that each of claims 44-45 each depend from claim 43 and are thus also patentable for the same reasons.

#### Reply to Claim Rejections – 35 U.S.C. §103

Claim 2 is rejected under 35 U.S.C. §103(a) over Hu et al. (*Genome Research*, 11(7):1237-45 (July 2001)) in view of Phillips et al.(U.S. Patent Serial No. 6,171,793); claims 5, 23, 29-30, and 38-39 are rejected under 35 U.S.C. §103(a) over Hu et al. (*Genome Research*, 11(7):1237-45 (July 2001)) in view of Wang et al. (U.S. Patent

Application Publication Serial No. 2002/0029113); and claims 13-15, and 32 are rejected under 35 U.S.C. §103(a) over Hu et al. (*Genome Research*, 11(7):1237-45 (July 2001)) in view of Helt et al. (*Genome Research*, 8(3):291-305 (1998)).

As described above with respect to the rejection made under 35 U.S.C. §102(b), Applicants respectfully assert that Hu et al. does not describe all of the limitations of independent claims 1 from which claim 2 depends, 3 from which claims 13-15 depend, and 28 from which claim 32 depends. Similarly, Applicants respectfully assert that neither Phillips et al. nor Helt et al. describe the combination of elements of each of the aforementioned independent claims either alone or in combination with Hu et al. Thus, Applicants respectfully assert that the combination of the disclosure of Hu et al. with Phillips et al. or with Helt et al. does not describe each of the combination of elements of claims 2, 13-15, or 32.

In addition, Applicants respectfully assert that, at the time the invention was made, the present application and Phillips et al. were commonly owned by Affymetrix, Inc. and thus should not be asserted in an obviousness rejection as per 35 U.S.C. §103(c).

Further, as described above with respect to the rejections made under 35 U.S.C. §102(b) and 35 U.S.C. §102(a) and (e), Applicants respectfully assert that neither Hu et al. nor Wang et al. describe each of the limitations of the independent claims 3 from which claims 5 and 23 depend, or 28 from which claims 29-30 and 38-39 depend. Therefore Applicants respectfully assert that neither Hu et al. nor Wang et al. describe each of the limitations of claims 5, 23, 29-30, and 38-39 either alone or in combination.

Therefore, Applicants respectfully assert that claims 2, 5, 13-15, 23, 29-30, 32, and 38-39 are patentable, and request that the rejections under 35 U.S.C. §103(a) be withdrawn.

### CONCLUSION

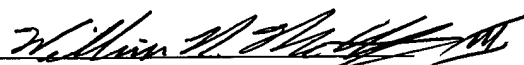
In conclusion, Applicants have amended each of claims 1, 3, 28, and 43 to include limitations that none of the references applied under 35 U.S.C. §102 or §103 disclose and thus respectfully assert that each are patentable. Further, since claims 2, 4-5, 7, 11-21, 24-25, 29-37, 40-41, and 44-45 each depend from one of claims 1, 3, 28, or 43 in their chain of dependency each are thus patentable for the same reasons.

For these reasons, Applicants believe all pending claims are now in condition for allowance. If the Examiner has any questions pertaining to this application or feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (781) 280-1522.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

By 

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Attachments

17 Replacement Sheets -Drawings  
Copy of Declaration



Application No.: 10/065,856

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